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Progress in Peripheral Vascular Surgery

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ARTERIAL DISEASES rank among the most common illnesses of man and each year are responsible for an increasing number of deaths.[1-3] Arteriosclerosis, the most common of these arterial diseases, has been the subject of intensive study and many factors influencing its progress and its severity have been discovered and in some cases controlled. This massive research effort has not discovered the basic etiologic factors but it has shown important features which have been extremely useful in the management of these problems.

During the past two decades this tremendous surge of interest has generated a widespread clinical and experimental effort. Such efforts have been aided by the development of sophisticated angiographic techniques which permit the safe and precise study of arterial lesions. During the same period, improvements in vascular surgical techniques allowed immediate application of newly acquired concepts, and the ensuing successes captured the attention and imagination of many surgeons. In addition to these stimuli, governmental agencies have encouraged and supported research concerning the cause and treatment of arterial diseases.

The histologic features of arteriosclerosis, although well described, have not disclosed significant clues identifying exact etiological factors.[4] The varying susceptibility of different segments of the arterial tree to arteriosclerosis suggests that certain inherent features of these particular arteries render them more vulnerable. Deficient blood supply of the arterial wall has been implicated as a critical factor, therefore perhaps partly explaining the increased susceptibility of the terminal aorta, which lacks vasa vasorum. It has been suggested that the histologic features of arteriosclerosis are consistent with the process beginning as degeneration of smooth muscle cells in the wall. This may be an example of cells responding in a uniform fashion to injuries incurred as a result of different types of trauma.[4] It has also been shown that changes in blood lipids, both in content and quality, can exert undesirable influences upon the progression of arteriosclerotic lesions. Similarly, prolonged hypertension has been shown to accelerate the rate of progression of arteriosclerosis, suggesting that control of hypertension might slow this progression. Despite this widespread effort, understanding of the exact relationship of these factors has yet to be acquired.

As a result of these studies, certain basic concepts emerged and have been of great value in the management of arterial diseases. Many studies have centered on the morphological characteristics of arterial diseases and the pathophysiological changes produced by the altered hemodynamics. With the rapid development of vascular surgical techniques it quickly became apparent that surgical methods of treatment were available which might be applied directly toward the restoration of normal hemodynamics, despite ignorance of the basic cause. As DeBakey pointed out, the segmental nature of arteriosclerosis produces well localized disease with a relatively normal proximal and distal arterial bed and allows vascular

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surgeons to "leap over the etiological wall" and effectively treat these patients.[1] Several important morphological features have been delineated and among these the tendency of arteriosclerosis to be segmental rather than diffuse is very important.[5] Moreover, arteriosclerotic plaques in their formative stages are eccentrically located within the arterial wall and thus a portion of the artery may be spared. These features immediately suggested that bypass techniques might be feasible, and a relatively normal arterial wall opposite to the plaque might be used as a base for attaching grafts. Application of these concepts was directly responsible for the rapid progress evidenced by vascular surgery. Findings of further studies showed that in some cases the arteriosclerotic lesions tend to become stable late in the disease. Results of successful bypass operations might, therefore, be quite durable if methods could be developed to control the progression of the disease.

Findings in such morphological studies also suggest that arteriosclerosis in large arteries has two basic forms.[1,5] In one variety, the disease produces stenosis and subsequent occlusion, and in the other, ectasia and aneurysms. In the latter instance, the disease is not characterized solely by the proliferation of the subintimal plaque, but by destruction of the integrity of the wall, disruption of the elastic lamellae, and finally ectasia and aneurysmal changes. In accordance with those physical laws governing the relationship between diameter and tangential pressure, such aneurysms continue to increase in size. In some patients, associated distal occlusive lesions are also present, which shows that these diseases may coexist. Despite these problems, those principles applied to treating the occlusive lesion can also be successfully employed in the management of aneurysmal disease because it also tends to be segmental rather than diffuse. Such observations have shown the variation in the histological and pathological features of arteriosclerosis. Although the dissimilar nature of the changes in the arterial wall in stenotic and aneurysmal disease suggest different causes, this is uncertain because both lesions may be present in the same patient.

Altered hemodynamic patterns produced by proximal arterial stenoses are quite similar regardless of the basic cause. Consequently, in patients who have arteritis or arterial dysplasia as a cause of stenosis, symptoms may be seen quite similar to those caused by arteriosclerosis. Moreover, similar syndromes may exist in association with arterial trauma or emboli and therefore may also respond to appropriate surgical techniques. It is apparent that the restoration of normal hemodynamics is of immediate significance, while the treatment of the underlying cause may be classified as a concept of long-term management. Control of progression of these arterial diseases is, of course, very important if results of the initially successful surgical procedures are to have long-term durability. As alluded to previously, control of certain metabolic and hemodynamic features may retard the progression of arteriosclerosis. Unfortunately, those factors influencing the progression of arteritis and arterial dysplasia are not known.

Diagnostic Tests

Functional evaluation of the hemodynamic disturbances in these patients is important in assessing the need for surgical operation and subsequently evaluating the success obtained by surgical repair. It has long been recognized, and recently emphasized, that the most effective and reliable noninvasive technique in evaluating such cases is accomplished by obtaining a careful history and performing a thorough physical examination.[6] Although the diagnosis of vascular insufficiency is relatively straightforward, the concepts of pressure measurement originally introduced by Winsor in 1950 have been useful in assessing the arterial supply to the extremities.[7] Utilizing plethysmographic techniques Winsor measured pressures in arteries of the extremities and correlated these pressures with arteriosclerotic disease of varying degrees of severity. He suggested that measurements of segmental pressure in afflicted extremities might be useful in detecting areas of stenosis, and he also constructed indices for comparison of pressures between the brachial and tibial arteries. This concept has been employed by many other investigators and led to the development of instruments to be used for measuring distal arterial pressure.[8-10]

The Doppler ultrasonic flow detector has been extensively used in these measures. Continuing efforts by bioengineers have resulted in the production and marketing of small, relatively inexpensive ultrasonic flow detectors which have proven useful for these studies.[11] These techniques offer qualitative rather than quantitative data, but

have been especially helpful in the postoperative period, and in screening certain cases before arteriography.

A pulsed ultrasonic flow detector has recently been topographically synchronized to present oscilloscopic images which may be photographed, in this way affording some visualization of the contours of the vessel under examination. Similar to the results of radionuclide imaging, the contours are relatively hazy and not as well defined as those obtained with high grade arteriography, but nevertheless these are useful screening procedures. Ultrasound has also been employed in the form of echo ranging equipment in which techniques have been developed to delineate masses by comparing the differences in sound absorption and reflection of adjacent tissue. This B-mode scanning has been particularly useful to vascular surgeons in detecting the presence of arterial aneurysms, and in following their subsequent enlargement.[12] In many patients valuable information can be gained with these studies, and they may occasionally substitute for arteriography.

The introduction of bioengineering as an integral part of patient management has led to the development of other instruments which have proven useful in vascular laboratories. Measurements of electrical impedance of the extremities also offer information regarding the vascular supply. Sophisticated plethysmographic equipment utilizing mercury strain gauges may be used to study pulse wave forms and measure segmental pressures, and thereby assist in detection of zones of stenosis.[13,14] These pulse volume recorders can be employed during exercise, thereby permitting examination of changes when the muscles are active. Such data are valuable not only in the evaluation of the severity of the symptoms of the patient, but also in assessing the effectiveness and the durability of surgical reconstruction. These techniques have, for example, confirmed Edwards' concept that reductions in pulse pressure occur during exercise because of decreased distal arterial resistance combined with a proximal inflow block.[15]

Newer methods of measuring isotope clearance have also been of value in assessing ischemia of the lower extremity. The injection of sodium 124 or Xenon 133 into the muscle of the extremities and measurement of subsequent clearance permits a nuclear radiologist to indirectly assess the efficiency of blood flow in the small vessels.[16] These techniques may also indicate an increased rate of isotope clearance occurring during exercise. Potassium 43 may be used to detect and identify ischemic areas in striated muscle, complementing clearance studies.[17] Because of the expense and complexity of these tests they have mainly remained in the vascular research laboratories and have not been as useful in the clinical setting as some other methods.

Nuclear radiologists have developed techniques for radionuclide imaging of vessels. In these studies technetium 99 is injected and simultaneous scanning with a scintillation camera is done to produce an image that reflects the contours of the vessels.[18,19] Although these techniques lack the definition and accuracy of high quality angiograms, valuable information may be gained and direct puncture or catheterization of the diseased arteries may be avoided. In most cases angiograms will subsequently be required for a final decision, but such radionuclide imaging techniques may form the basis for a screening examination which in some patients may satisfactorily substitute for arteriography.

It has been amply shown by Linton, Edwards and others that arteriography is not always necessary for the diagnosis and management of patients with aortofemoral disease.[2] Nevertheless, high quality arteriograms are very useful and in some cases indispensable in making these judgments. Some studies are particularly helpful in planning vascular reconstructive procedures and in many cases postoperative arteriograms are essential. Following the early efforts in angiography by Brooks, Dos Santos and Moniz, these procedures have proven to be safe and very valuable.[20-22]

Translumbar aortography has been the most popular and useful technique for evaluation of the aortofemoral tree and continues to be used in many vascular centers. The extensive experience obtained with translumbar arteriography, and subsequently reported by Beall, DeBakey, Crawford and colleagues, outlined the basic principles of the procedure, and proved its safety and effectiveness.[23] Complete visualization of the infrarenal aorta, iliac and femoral-popliteal systems is essential in most cases, and can be readily obtained with techniques developed many years ago. The safety of a properly conducted translumbar

arteriogram has been repeatedly shown and the information obtained from these studies is very useful.

The Seldinger technique of percutaneous catheterization of major vessels added another dimension to arteriographic studies and continues to gain in popularity.[24] These techniques offer new versatility and allow the vascular radiologist through a single arterial entry to examine many portions of the arterial tree. The development of flexible and flow directed catheters and improvements in x-ray equipment have permitted catheterization and visualization of even small splanchnic arteries. Although at present quantitative data are not obtained, qualitative evaluation of flow patterns can be ascertained and are useful in assessing the severity of arterial lesions. The safety of these carefully conducted studies allows repetitive examination to be done and has permitted a broadening of the indications for arteriography.

The administration of microspheres and vasoactive agents and the visual examination of the effect upon distal vessels may offer valuable information as to the functional integrity of smaller vascular beds. Immediate visualization of the effects of certain drugs promises to be of use in the development of new therapeutic modalities to control and regulate the distal circulation. Specific efforts to treat congenital arteriovenous fistulae by direct embolization using these catheters has been successful in a number of cases and promises an increasing range of applicability.[25]

Arteriography either by direct puncture or by percutaneous catheter techniques is indispensable in the diagnosis and management of occlusive disease of the visceral and cerebral vessels.[26-28] Sophisticated biplane studies are often necessary to expose small ulcerative plaques and to correctly identify obstructive lesions. The safety of these techniques has been repeatedly shown and several series reflect thousands of arteriograms carried out with low mortality and morbidity.[29,30] Following the introduction of newer and better contrast media for arterial arteriography, previously seen complications of renal failure and spinal cord damage became extremely rare. It is now apparent that with the current techniques and proper precautions these complications no longer pose a significant threat.

Arterial entry of any type carries with it the possibility of damage to the arterial wall which may cause localized thrombosis and in some cases embolization. This is more likely to occur in percutaneous catheter studies, in which the catheter may become ensheathed with clot during a prolonged procedure, and as the catheter is removed the thrombus is stripped off and remains within the vessel. This is an unusual occurrence as shown in Lang's collected series of more than 11,000 arterial entries, with 81 major and 325 minor complications, and a total of four deaths.[29] This is also reflected in Mortenson's series, which again shows the relative safety of these procedures.[30] From the national cooperative study on cerebral vascular disease, in which more than 4,700 studies of cerebral vessels were undertaken, serious complications occurred in only 1.2 percent of the patients.[28] More recent data indicate that cerebral vascular arteriography under proper conditions carries a risk of inducing a serious neurological deficit or of producing a lethal complication in less than 0.1 percent of the studies.[31] Vascular radiology has emerged as a growing specialty because of these many refinements in safety and technique and the indications for its use have increased at a rapid rate.

The recent development of a computer controlled and analyzed method of x-ray tomography promises to change many diagnostic techniques.[32] Computer tomography basically consists of computer analysis of the amount of x-ray absorption by various tissues. The beams are precisely passed through the area to be examined; the amount of irradiation absorbed is dependent upon the type of intervening tissue or substances. Differentiation between ischemic and hemorrhagic infarcts may be possible with this technique. Blood clot can be easily identified, and therefore intracranial lesions may be better exposed with this test than other noninvasive methods. The management of cerebrovascular insufficiency is certain to be significantly influenced by this innovative technique.

Arterial Grafts

Since the introduction of the plastic graft by Voorhees and his associates in 1952, arterial prosthetic implants have undergone many changes, but it is obvious that the ideal substitute has not been discovered.[33] Currently the most commonly used grafts are constructed of knitted Dacron® yarn, but in some instances knitted and woven Teflon® are also employed. The porosity is adjusted to permit the ingrowth of fibroblasts in an attempt to support formation of a neo-intima. It

is clear, however, that the new lining of these grafts usually consists of impacted fibrin and in most cases is not a living cellular layer. Some ingrowth over the suture lines of each individual graft may occur, but complete healing of the graft is not often obtained. Nevertheless, Dacron prosthetic implants have been extremely useful and the experience reported from many vascular services has suggested that these are the most acceptable of the available plastic grafts.[34]

Recent experiences, however, warn that the long-term behavior of these grafts may be less reliable than originally thought.[35-37] Aneurysm formation, loss of tensile strength and fiber breakage have appeared and such failures, although quite rare, suggest manufacturing defects or biodegradation. In other instances mechanical trauma during processing or implantation has been thought to cause late failure. Of more etiological importance may be the techniques in which chemical shrinkage of the knitted graft is induced to increase the porosity. These methods may cause a significant loss of tensile strength, and when utilized to produce the higher degree of porosity thought to be desirable, stiffness and brittleness of the Dacron fibers may supervene. Such changes in the graft would appear to seriously compromise the long-term integrity of these implants. Edwards, the originator of the Teflon graft, has continued to suggest that it may be less susceptible to these influences.[38] These reports of failure of Dacron grafts lend credence to this suggestion, and strongly indicate that a reappraisal of the characteristics of the currently employed arterial implants be undertaken.

Sauvage has described the construction and utilization of a Dacron filamentous graft that supports living pseudointima consisting of fibroblasts.[39] The basic aim underlying development of this graft was to provide for the migration of fibroblasts a trellis along which cells could be directed toward the lumen of the arterial prosthetic implant; there they would form and support a living surface which would be relatively electronegative and less favorable to late thrombosis. The long-term behavior of this graft should be more reliable if such a lining can consistently be induced, and preliminary reports suggest that this may be possible. In addition, the healed external capsule may offer support to the long-term integrity of the wall of these Dacron grafts. Wesolowski, Sauvage and many others continue the intensive investigation into the acquisition of artificial prosthetic materials which are more acceptable for arterial implants.[40,41]

Recent advances in the development of plastics have led to the suggestion that expanded polytetrafluroethylene may be molded into an arterial implant which embodies many of the desirable characteristics alluded to in the previous section.[40] These grafts also have a filamentous design to assist in the orientation and migration of fibroblasts, and moreover, seem to lack the intense thrombogenicity seen in Dacron grafts. Early reports from vascular centers studying these newer materials suggest that even small grafts may be utilized, a characteristic not shared by Dacron and Teflon, and therefore they may be eventually useful as aortocoronary bypass grafts when suitable saphenous veins are not available. Enthusiastic reports of early successes in the experimental laboratories and in a few instances in patients have stimulated an intensive investigation. If these early reports prove to be well founded a new era in arterial grafting may be opened.

Initial efforts to secure other grafts to be utilized in those patients in whom autogenous tissue was not available were relatively unsuccessful because of lack of tensile strength and thrombotic tendencies of the finished products. In many cases collagen tubes were fabricated, following the lead of Schilling, Sparks and others.[42,43] Dies were placed in the subcutaneous tissues to incite and direct the growth of an autogenous collagen tube that might be used as an arterial implant. These procedures have been useful in certain cases but their versatility is limited by the fact that in many instances the relative urgency of the procedure does not allow time for growth and harvest of an autogenous collagen tube.

Because of these reasons Rosenberg, Keshishian and others looked into the possibility of acquiring heterografts and treating them to reduce their antigenicity and to increase their tensile strength.[44-46] The current preparation, bovine carotid artery, is satisfactory in most cases. The artery is first digested by ficin, leaving a residual collagen tube, which is tanned with dialdehyde starch to increase its tensile strength. This graft has been very useful in many cases, especially in those patients in whom there was not a suitable saphenous vein. It carries the obvious advantage

of not requiring pre-clotting and appears less susceptible to the dense fibrous incapsulation and rigidity which unfavorably influences the long-term behavior of plastic prosthetic implants. These bovine heterografts have also been used in the construction of arterial-venous fistulae for hemodialysis and intravenous hyperalimentation. Such heterografts tend to retain their integrity despite numerous punctures. In certain cases localized aneurysms have occurred but some of these have been successfully resected and graft segments interposed to restore continuity and thus salvage the conduit. Studies in these patients have shown a low order of graft antigenicity. These preliminary data suggest that bovine grafts may be more satisfactory than plastic arterial substitutes in the lower extremities.

Vein Grafts

One of the major factors limiting the long-term success of saphenous vein bypass grafts has been primary vein failure. Early studies of aortocoronary vein grafts indicated a low but significant attrition rate due to an intense fibrosis causing thrombosis. These problems have not been common in vein grafts placed in the aortorenal, femoral-popliteal or femoral-tibial position, but localized areas of damage and subsequent stenosis or thrombosis have been described. Reports by Szilagyi, Stanley, Dean and their associates have shown that injuries incurred at the time of harvest of the saphenous vein may be responsible for many of these untoward effects.[47-49] Ischemia and hypoxia may also damage the vein and predispose it to fibrosis, stenosis and subsequent thrombosis. In addition, injury produced by rough handling may produce discrete lesions in the vein which ultimately lead to stenosis.[50] There is highly persuasive evidence that the thrombosis may occasionally begin on the distal side of the valve cusp where there is early aggregation of platelets and fibrin deposition.

In many cases harvesting of the autogenous vein has been left to the more junior person on the surgical team and it was inevitable that proper handling of the vein might not be achieved in all cases. Recent studies suggest that certain precautions should be taken when removing the veins for use as arterial implants; these include minimizing the warm ischemia time and avoiding overdistension and the use of crushing clamps—which may cause intimal damage.[50] The vein should be left in its natural bed until just before use, keeping the ischemia time to a minimum. If there is delay before insertion the vein should be handled as an allotransplanted organ and protected by hypothermic perfusion with balanced crystalloid or colloid solutions. It has been suggested that perfusion of the vein may best be accomplished with a cold heparinized autogenous solution of whole blood, particularly if it is necessary to remove and store the vein for even short periods.[48] These precautions cannot be overemphasized since vein grafts are being inserted with increasing frequency in almost every major hospital in the United States.

Studies investigating the late behavior of saphenous vein autografts have revealed a curious phenomenon. Some 15 to 20 percent of saphenous vein aortorenal grafts tend to increase in diameter, and in 4 to 6 percent of cases true aneurysms have occurred. Stanley, Dean and their associates have suggested that this may be a reflection of the increased velocity of blood flow to the kidney.[48,49] Lack of surrounding tissue support has been indicted, but this is also a feature of aortocoronary grafts, and these tend to become stenotic rather than aneurysmal. There are currently in progress intensive and urgent investigative efforts directed toward elucidating these phenomena. Serial angiographic studies are being obtained in order to carefully follow these changes in venous autografts. It is apparent that a considerable amount of work is yet to be done if such untoward late effects are to be removed and long-term function of these grafts improved.

Adjunctive Methods

Heparin has been extremely useful in many phases of vascular surgery, but specific indications and methods of administration have repeatedly changed during the past decade.[51] Heparin is obtained from beef lung or porcine gut and its potency is somewhat stronger in the latter preparation. It has been shown to exert its anticoagulant effect by inhibiting factor seven and factor nine, and also acting as an antithrombin. In higher doses it interferes with the thrombin-platelet interaction and the subsequent release reaction. It apparently has a biphasic action and in low doses does not change platelet stickiness, but in the high ranges may inhibit platelet aggregation.[52] It is an anti-inflammatory and an anti-aldosterone agent, and also has the ability to inhibit serotonin release and to induce clearing of blood lipids.[53] Recent studies strongly suggest that

the most favorable mode of heparin administration is by the continuous intravenous route utilizing a pump for steady infusion.[54] This technique is apparently safer and the therapeutic effects may be obtained with a lower overall dose. Tighter control is achieved and thus the more significant bleeding complications occur less commonly. Intermittent intravenous injection is also useful in certain cases, but apparently is accompanied by slightly more common side effects.[54]

There is persuasive evidence that the administration of smaller amounts of heparin, 5,000 units administered every 8 to 12 hours, may reduce the incidence of deep vein thrombosis and subsequent thromboembolic phenomena, particularly in high risk patients.[55] This appears to be the result of potentiation of factor Xa inhibitor, a natural anticlotting agent. Other studies dispute the efficacy of heparin in these situations. It is clear that the effectiveness of heparin in such patients is not yet decided.

Heparin is clearly of great value in vascular surgery, and this is especially true in the initial management of patients with arterial emboli, and during operations on renal and cerebral arteries. Most surgeons also utilize heparin during operative procedures on other parts of the arterial tree, especially femoral-popliteal, tibial and occasionally aortoiliac and aortofemoral vessels. Postoperative anticoagulation is rarely employed in most vascular clinics because heparin has been shown to occasionally induce serious bleeding and is associated with a higher incidence of wound infections. Moreover, there is little evidence that heparin will salvage a poor vascular repair, and most vascular surgeons believe that a satisfactory arterial reconstruction does not require postoperative anticoagulation.

It has long been recognized that plasminogen activator is present in greater concentration in the walls of veins and pulmonary arteries than in the walls of systemic arteries, especially larger and less muscular ones. The natural history of clots in the venous and pulmonary system has been one of spontaneous lysis and recanalization.[56] This is an unusual occurrence in systemic arteries and is thought to be due to this relative lack of plasminogen activator in these vessels, but perhaps is also influenced by the progressive stenosis of arterioclerosis. Because of this disparity in normal fibrinolysis, there have been many efforts to initiate clot lysis by the administration of other activators. This has largely centered around the use of streptokinase and more recently urokinase. Initially these activators were difficult to use because of their antigenicity, cost and lack of standardization. Early preparations were unsatisfactory but interest continued in the experimental laboratories. With recent manufacturing improvements, a preparation was developed which could safely be employed in a controlled patient study. The study was initially concerned with pulmonary emboli, and in a multidisciplined cooperative protocol lysis was achieved by a carefully regulated course of intravenous streptokinase.[56] Findings on pulmonary angiographic studies indicated that administration of this activator did indeed shorten the time required for clot lysis, but mortality analysis showed that there was no significant change in patient survival. Urokinase, apparently safer but more expensive, has not been available in sufficient quantities to assess its efficacy, although numerous studies are currently in progress.

Because of the success achieved in hastening lysis of clots in the pulmonary circulation it has been suggested that streptokinase might be useful in the management of arterial emboli and thrombosis.[57] Unfortunately establishment of satisfactory protocols for its evaluation is difficult because in many of the patients concerned, thrombosis may ensue in the immediate postoperative period when it is hazardous to administer a plasminogen activator. This is particularly true following major vascular procedures. On the other hand, those patients in whom thromboembolic phenomena and threatened viability of an extremity are present are not suitable candidates for the administration of an agent whose effect is necessarily delayed. In many cases viability of the extremities will be measured in hours and direct intervention will be required if tissue loss is to be prevented. Despite the initial enthusiasm, activation of the endogenous fibrinolytic system in the management of thromboembolic disease has not been as useful as hoped. In previous studies the activator was administered directly into the artery in an attempt to localize its effect and intensify its ability to induce clot lysis. Perhaps the newer arterial catheterization techniques may be mobilized in this area, and when joined with the administration of plasminogen activator, procedures may be developed which would permit clot lysis in patients with acute thromboembolic phenomena.

Adjunctive Methods—Platelets

It has been established, especially in the cerebral circulation, that platelet emboli originating in arteriosclerotic ulcerative plaques are an important cause of distal arterial obstruction.[58] There is also persuasive evidence that adherence of platelets to endothelium results in endothelial damage which may be related to subsequent arterial thrombosis. Methods of inhibiting the aggregation of platelets are under intensive study, and it has been shown that certain agents interfere with this phenomenon. In platelet aggregation two basic reactions are involved: the stimulus presented by exposure of platelets to collagen and the aggregating effect of adenosine diphosphate—released as a result of the initial surface reaction. Certain groups of chemicals have been shown to inhibit these reactions and are generally divided into three types. Tricyclic compounds include some antihistamines and tranquilizers, but the mode of action is not clear. The pyrimidopyrimidine compounds act by interfering with the adenosine diphosphate (ADP)-induced platelet aggregation. The most commonly employed representative of this group is dipyridimole. The third group of drugs, the nonsteroidal anti-inflammatory agents, include sulfinpyrazone and aspirin.[59]

Aspirin is considered useful in blocking the surface release reaction of platelets and may also interfere with secondary ADP-induced aggregation. It also inhibits epinephrine-induced release of ADP; collagen and ADP-induced activation of platelet factor IX. It does not impair the response to thrombin. These drugs may therefore be initially useful in the treatment of arterial diseases which are accompanied by platelet emboli. They may also be of value in inhibiting the aggregation of platelets in the immediate postoperative period after vascular reconstruction. Their prophylactic effect continues to be disputed both in arterial and venous diseases because of conflicting reports, reflecting in many cases differences in protocols and study techniques.[60] Cooperative studies are currently in progress to ascertain the effectiveness and mechanisms of action of these agents. Preliminary reports by Salzman, Silver, Evans and others strongly suggest that these agents will be extremely useful both therapeutically and prophylactically in vascular surgery.[60] At the present time, however, the exact indications for use and modes of action remain unclear.

Aortoiliofemoral Occlusive Disease

During the past two decades a tremendous amount of experience in the management of occlusive aortofemoral disease has been accumulated. A unique opportunity to construct a profile of vascular occlusive disease has been offered vascular surgeons. This is largely the result of the opportunity to correlate symptomatology, physical findings and angiographic illustration of the lesions with the direct operative examination of morphologic and histopathologic characteristics.

Arteriosclerotic lesions of the vessels supplying the lower extremities tend to be distributed in such a fashion as to spontaneously separate into three groups.[1,5] The first, aortoiliac disease, is characterized by primary involvement of the terminal aorta, the common iliac and hypogastric arteries. The disease usually tends to end in the proximal 1 or 2 cm of the external iliac arteries. Patients with this "pure" form of aortoiliac occlusive disease are younger, tend to have less widespread and less severe arterial disease and have milder symptoms.

More commonly the distribution is aortofemoral and involves the entire infrarenal aorta and the iliac system, and plaques are also found in the common femoral, the profunda femoris and the superficial femoral arteries. Segmental accentuation is present but less distinct in these patients. As expected they are somewhat older and have more diffuse arterial disease. These people also have more severe associated symptoms, especially from lesions present in the coronary, renal and cerebral arteries. Associated hypertension is present in almost half of these patients, myocardial disease in a third and cerebrovascular and renal disease in approximately 10 and 15 percent respectively.

In the third variety the major plaques are in the femoral, popliteal and tibial system. In these patients the lesions are most severe in the superficial femoral artery as it traverses the adductor canal, but also involve the popliteal, especially in its mid and terminal portions. The orifices of the tibial arteries are often stenotic. These patients tend to be somewhat younger than those encountered in the aortofemoral group, and often have diabetes or lipid disorders or both. Of course, in its more severe forms, the separation is less distinct. One may, therefore, expect to encounter combinations in many patients. It has been shown, however, that in only 10 to 15 percent of patients having

successful aortofemoral repair will femoral-popliteal reconstruction be required subsequently.[61,62]

The clinical syndromes which eventuate as a result of arteriosclerotic lesions of the aortofemoral system can be roughly divided according to their severity. Those patients with a "pure" form of aortoiliac stenosis and with the milder forms of aortofemoral or femoral-popliteal lesions often present with mild ischemia, characterized by claudication. This claudication may be slowly progressive and the severity of the ischemia may increase, but in many instances it remains relatively stable for long periods. In only a small proportion of patients is amputation eventually necessary. In its most severe form, however, the ischemia produces disturbances in tissue nutrition which eventuate in ischemic rest pain, and if untreated, gangrene. The importance of assessing the functional significance of these lesions cannot be overemphasized since they often yield to established vascular procedures. Nevertheless, the eventual outcome in these patients is more often determined by the severity of associated arterial disease, particularly when coronary and cerebral vessels are involved.

The operative management of occlusive disease of the aortofemoral tree basically employs one of three techniques, or various combinations. Thromboendarterectomy, employing autogenous tissue and thus excluding the need for graft implantation is appealing and has been successfully used in many cases. This technique unfortunately cannot be applied to all cases, and is usually limited to those patients who have relatively localized disease of the aortoiliac tree. Arterial aneurysms or vessels with severe calcification involving the entire wall of the artery are not suitable for this technique. Disruption of the artery and early thrombosis are often seen in these cases. Other problems are encountered with long endarterectomies of the superficial femoral and popliteal arteries, which may be followed by an intense fibrotic reaction. Accumulated experience has indicated that aortoiliac endarterectomy is a useful technique, but when the disease is more diffuse and involves the entire aortofemoral tree, bypass grafting is easier and just as successful. Careful analyses presented by Szilagyi, Gaspard, Stoney and other workers indicate that little difference can be shown in the success and durability of aortofemoral grafts in comparison with aortofemoral endarterectomy.[61-64]

Although the morbidity following these procedures is approximately 20 percent, mortality rates of 2 to 4 percent are regularly reported. Five- and ten-year studies of patients having undergone aortofemoral reconstruction show the operation to be remarkably durable, considering the disease encountered in some patients. Continued patency rates of these repairs in 70 to 80 percent of patients have been repeatedly shown.[65,66] Those patients with disease limited to the aortoiliac segment regularly exhibit five-year patency rates in excess of 85 percent, but as expected the operations are less successful in those patients with aortofemoral disease and especially if there are associated femoral-popliteal occlusive lesions.

Femoral-Popliteal and Tibial Disease

In some patients with vascular insufficiency of the lower extremities the predominant arteriosclerotic lesions will be found in the femoral, popliteal and tibial vessels. This is particularly likely to occur in patients with diabetes mellitus, thromboangitis obliterans and various lipid disorders. In addition, there is a group of relatively young adults in the third and fourth decades of life who appear to have an increased incidence of femoral-popliteal arterial disease, but in whom no specific causes have been found.[67]

Certain basic patterns of involvement are frequently encountered and it has been repeatedly observed that the superficial femoral artery as it passes through the adductor canal is extremely susceptible to stenosis and occlusion. Haimovici observed and reported on the patterns of arteriosclerotic involvement of lesions in the lower extremity and these data offer useful guidelines for study of this disease.[68] Subsequent reports by Morton and co-workers characterized the patterns of tibial disease associated with arteriosclerotic involvement of the popliteal artery, and related these changes to the possibilities of successful reconstruction.[69] Reports by Linton and Darling, and Crawford and his colleagues confirmed the pattern of involvement which characteristically includes occlusion of the superficial femoral artery and reconstitution of the distal popliteal and tibial vessels.[67,70]

The diagnosis of disease of the femoral-popliteal and tibial vessels is relatively simple in most cases because direct examination of the superficially located arteries is possible. Plaques can

often be palpated in the femoral vessels and occasionally in the anterior and posterior tibial arteries. It is relatively simple to detect diminished pulses, bruits, and zones of stenosis and obstruction. Measurements of distal pressure and flow as originally conceived by Winsor may be of value in the assessment of these problems, but in most cases complete angiographic evaluation is necessary in order to properly plan the method of vascular repair.

The indications for operation in patients with femoral-popliteal disease and vascular insufficiency of the lower extremities must be carefully evaluated and stringently applied. It is a rare happening in a patient with claudication caused by aortofemoral disease for loss of an extremity to occur as a complication of surgical operation, but this is more of a threat in femoral-popliteal and femoral-tibial reconstructive efforts.[71] The initial determination of the need for operation must be balanced against the hazard attending the procedure. It is apparent that in those patients with diffuse tibial disease and a reduced outflow tract the likelihood of technical success diminishes and the risk to the extremity increases.[72] Most surgeons limit femoral-popliteal and femoral-tibial bypasses to those patients in whom there are symptoms of vascular insufficiency that are so severe as to interfere with normal day-to-day activity and preclude their being gainfully employed. In patients in whom rest pain and other signs of severe ischemia are present, surgical repair is necessary in order to assure viability of the extremity. It is apparent, however, that in those instances in which technical repair cannot be successfully accomplished, changes in cardiac function, increased metabolic demands placed upon the operated extremity and the interruption of vital collateral channels may precipitate loss of the limb. In these patients, therefore, the indications for operation should be very strong. This is especially true if it is feared that satisfactory conclusion of the operation may not be achieved because of inherent technical difficulties.[72]

In the usual operation the reversed saphenous vein is placed from the common femoral to an appropriate position in the mid or distal popliteal artery and occasionally to one of the tibial arteries.[73] These procedures are accompanied by common and profunda femoral thromboendarterectomy if these arteries are significantly compromised by arteriosclerotic plaques. In some cases composite grafts may be constructed of a combination of saphenous vein and tube plastic grafts, or sections of bovine heterograft. This may be necessary in those instances in which the saphenous vein is of insufficient length and other autogenous veins, such as the cephalic vein, are not available. The studies presented by Mannick and others suggest that the distal anastomosis may on occasion be made to an isolated popliteal artery, without patent tibial arteries, and yet success be achieved in up to 50 percent of patients.[74] Most surgeons, however, would favor in this situation extending the graft distally and attaching it end-to-side to a tibial artery, thus bypassing all the proximal lesions.

The data developed by Mannick also showed that after bypass grafting an additional increase in blood flow could be obtained by adding a lumbar sympathectomy.[75] It is apparent, however, that in and of itself sympathectomy is of much less value than an adequate reconstruction, and if sufficient flow through the graft can be obtained initial patency in nine out of ten patients has been reported. In those patients with a satisfactory outflow tract (that is, two or three patent tibial vessels), five-year patency rates of 80 percent have been reported. Several series at ten years report continued patency of up to two thirds of the grafts. The operative mortality is usually low and such long-term successes have generated a considerable amount of enthusiasm for these operations. There are dissenting reports, however, by Stoney and Martin and their colleagues.[72,76] These workers have suggested that the attrition from associated arteriosclerotic vascular disease is of such magnitude that the ultimate limb salvage in the patients with severe ischemia is quite low, 25 to 35 percent at five years. These somber reports suggest that a reappraisal of the usefulness of this operation be undertaken. It is difficult to reconcile these conflicting reports from established vascular clinics, each with a great deal of experience.

The debate as to the effectiveness of this procedure is further compounded by the studies of Garrett, and Tyson and Reichle and their associates.[77-79] These workers have shown that femoral-tibial bypass grafts utilizing the reversed saphenous vein are quite effective in patients in whom femoral-popliteal grafts were not feasible. Reports by these surgeons suggest that construc-

tion of these bypasses may be somewhat more difficult but initial success rates may be achieved in approximately 50 percent of patients. The long-term behavior of the grafts is quite good, and five-year patency rates of 75 percent have been reported. Limb salvage in many cases has been dramatic and in most patients the operation is proposed only as an attempt for limb salvage.

There is less enthusiasm for thromboendarterectomy of the superficial femoral and popliteal arteries, although in some cases localized plaques may be removed by this technique. Findings in numerous studies done in the last decade have shown that although initial patency following femoral endarterectomy is quite high, the procedure may not be as durable as vein grafting. These techniques may be required in some patients when autogenous veins are not available, but in most cases the majority of vascular surgeons prefer to utilize knitted Dacron or bovine heterografts as a femoral-popliteal bypass graft rather than carry out a long endarterectomy. Crawford has reported that in those cases in which 8 mm knitted Dacron grafts are inserted in the femoral-popliteal position patency rates quite similar to those reported with reversed saphenous vein can be achieved.[80] For plastic grafts to remain patent a better outflow tract is required and it appears clear that these prostheses are less desirable and although initially successful cannot be expected to be as useful as the reversed saphenous vein.

Bovine heterografts are favored by many vascular surgeons.[44] They have the obvious advantages of not requiring preclotting, and they are pliable and easier to handle than plastic grafts. The available sizes are limited, but 6 or 7 mm grafts are very useful in femoral-popliteal operations. The long-term behavior of these grafts, like plastic implants, appears less satisfactory than that obtained with vein grafts. Their major utility would seem to be in those patients for whom a satisfactory autogenous vein is not available.

Abdominal Aortic Aneurysms

Arterial aneurysms are common manifestations of generalized arteriosclerosis. It is estimated that 2 to 4 percent of the general population over 25 years of age have abdominal aortic aneurysms, but they usually occur in people in the sixth or seventh decade of life. Males outnumber females by a nine to one ratio.[81] In most instances the abdominal aortic aneurysms are fusiform and in 98 percent of cases are distal to the renal arteries. Other causes of aneurysms include syphilis, trauma, sepsis and inherited arterial disorders, such as Marfan's syndrome. Segmental accentuation, as seen in the occlusive forms of arteriosclerosis, is also present, but less pronounced in patients with arterial aneurysms. There is a great tendency for concomitant involvement of the iliac arteries when an abdominal aortic aneurysm exists and it is not rare to also encounter in the same patient aneurysms of the common femoral and popliteal arteries. When these combinations do occur, bilaterality is frequent and may further complicate the management of these cases.

The natural history of abdominal aortic aneurysms has been elucidated by many studies. Initial reports by Estes and Wright suggested that most of these lesions inexorably increased in size, and approximately 40 percent eventually ruptured.[82,83] These authors further stated that the five-year survival of untreated patients with abdominal aortic aneurysms greater than 6 cm in diameter was less than 10 percent. These initial studies were not accompanied by satisfactory controls, but Szilagyi and co-workers have examined the natural history of these lesions utilizing actuarial protocols and life table methods.[84] These studies contained a matched series of patients from which two groups, one treated surgically and one not treated surgically were prospectively evaluated in regard to morbidity, rupture and survival. These data confirmed the initial impression that aneurysms greater than 6 cm in size were more dangerous than smaller ones, although rupture was not confined to large aneurysms. It has therefore been established that over 35 percent of aneurysms greater than 6 cm in diameter rupture and cause an alarmingly high morbidity and mortality. In fact, of 280 patients in whom resection was not undertaken because of various nonmedical reasons the five-year survival rate was only 6 percent, while in over 400 comparable patients who had elective abdominal aneurysmectomy the five-year survival was 47 percent, including operative mortality. These studies also showed that the rupture rate was significantly higher in patients with sustained hypertension.[84,85]

Although initially thought to be infrequent, recent reports have suggested that distal embolization may occur in up to a third of the patients

with aortic aneurysms.[86] Such epidemiologic studies clearly strengthen the rationale for excision of large aneurysms in patients in whom the risk of surgical operation is not prohibitive and the outlook for continued survival is reasonable.[87] This is especially important if the patients have sustained hypertension.

The diagnosis of peripheral arterial aneurysms is made on physical examination in most cases, but in some instances may require arteriography for confirmation. Newer techniques employing echo-ranging equipment are useful in determining size and rate of growth of these aneurysms. In fact, the B-mode ultrasonic scanning has been shown to accurately measure aneurysm size in many patients.[12] Findings on plain x-ray films may indicate the presence of calcification and correlate with clinical findings, but in some instances these studies fail to show the aneurysm. Because of the occasional involvement of associated visceral arteries, particularly renal and mesenteric, aortography is being used more often. Many surgeons believe that most cases should be angiographically examined in order to plan the operative management, and to assess the visceral and distal circulation before surgical operation. Despite the validity of these indications, most abdominal aneurysms are diagnosed clinically, and usually resected without the benefit of angiography.

The operative management embodies those same principles that are employed in the management of occlusive disease of the aortofemoral tree. Early efforts to induce thrombosis by wiring and ligation or to control expansion by aneurysmorrhaphy have largely been supplanted by resection and graft replacement. By far the most common procedure currently employed in the surgical management of abdominal aortic aneurysms is resection and graft replacement. In most cases the aneurysms are isolated and after removal of a portion of the anterior wall of the aneurysm the graft is sewn to the aorta just distal to the renal arteries. The distal limbs of the graft are attached beyond the disease to either the iliac or the femoral vessels.

In the elective situation these procedures are highly effective and mortality rates as low as 4 percent have been reported from centers experienced in surgical management of aneurysms.[12,81,84] In contrast are those patients for whom operations must be undertaken in the face of an acute rupture. Mortality rates in excess of 50 percent are almost always encountered.

Sepsis

Of the complications which may occur following prosthetic grafting, one of the most distressing is that of infection of the anastomosis. Infection of the shaft of the prosthetic implant may occasionally yield to appropriate antimicrobial therapy and drainage, but as shown by Szilagyi, Smith, Elliott and associates, postoperative infections which involve the anastomotic line or the neointima are rarely successfully managed without removal of the prosthetic implant.[88,89] These complications are extremely hazardous both to the patient's life and to the survival of the afflicted extremities. Graft infections are fortunately very rare and several large clinics have reported an incidence of 1½ to 3 percent. Once anastomotic infection is present, false aneurysm, thrombosis and bleeding are the rule, and if early intervention is not successful loss of the limb or a fatal outcome can be expected.

The concepts of establishing remote bypasses through clean tissue planes before removal of the infected prosthetic implant were originally promoted by Blaisdell and Hall, and Shaw and Baue.[90,91] The importance of these principles cannot be overemphasized. Axillary-femoral, femoral-femoral and obdurator bypasses have been extremely useful in the successful management of these very difficult problems. Surprisingly, these relatively circuitous bypasses have proven to be fairly durable. The studies of Brief and others have illustrated that the five-year patency rates of femoral-femoral bypasses exceed 70 percent.[92] More than half of the axillary-femoral bypasses may be patent after two years, particularly if a femoral-femoral limb to the other side is added, thus increasing the volume of outflow. The ability to supply needed blood flow to the distal extremity before removal of the infected prosthetic implant has enabled the vascular surgeon to successfully manage problems which previously produced alarmingly high mortality rates.

Arterial Emboli

During the past two decades, arterial emboli have continued to present significant problems in diagnosis and management, but basic etiological factors appear to be changing.[93] For many years the most common causes of arterial emboli were congenital and acquired cardiac defects, and arrythmias. Prevention and correction of many cardiac defects have significantly reduced those

cases which eventually are complicated by arterial embolization. Cardiac arrhythmias continue to cause arterial emboli and are most often seen in association with arteriosclerotic heart disease. Myocardial infarcts with associated mural thrombi constitute another important source of emboli and it is therefore believed that most arterial emboli are of cardiac origin and are the direct result of arteriosclerotic heart disease. The insertion of prosthetic devices into the heart may lead to the generation of platelet aggregates and fibrin accumulations which may embolize. Emboli of platelets, fibrin and atheromatous debris may also emanate from ulcerative lesions in arteries afflicted with arteriosclerosis.[94] This is a common cause of cerebral vascular dysfunction.

One of the most important developments to appear during the rapid progress of vascular surgery in the past 15 years has been the introduction by Fogarty of balloon tipped catheters for extraction of clots.[95,96] These instruments have allowed removal of arterial emboli with a facility heretofore not possible. The importance of the techniques developed as a result of those studies leading to the Fogarty catheter cannot be overemphasized. Embolectomy under local anesthesia has become a common and successful method of extraction of intraarterial clots. Relief of arterial obstruction with minor operative procedures is in sharp contrast to the surgical techniques previously required to restore arterial continuity. The lower operative risk, successful extraction of clots, reduced operating time and wide applicability of this technique have resulted in less patient morbidity and in some cases a dramatic reduction in patient mortality. Of course, if the basic cause of the arterial embolization is not removed the patients are subject to recurrent episodes and may eventually die from the underlying cardiac disease that was responsible for the generation of the emboli. Nevertheless, these catheter techniques have had a pronounced influence not only in the management of thromboembolic disease but also in those procedures associated with *in situ* thrombosis. Reoperation with distal clot extraction has been made possible by these simple, more efficient techniques.

The aggressive application of the Fogarty catheter extraction of clots has inevitably resulted in some arterial damage and certain precautions must be observed if these procedures are to be successfully pursued.[96] Despite the relative fragility of the latex balloon, arterial rupture is possible and has been reported. In addition, repeated passage of the balloon produces intimal injury, and the tendency of the arterial wall to respond to injury by the deposition of arteriosclerotic plaques is well known. Intramural dissection, perforation, fragmentation of the balloons, kinking, difficult extraction and clot dissemination have been described. It is also obvious that antegrade removal of clots using balloon tipped catheters may because of the "snow plow" effect obstruct collateral channels. Despite these shortcomings, many of which can be overcome with proper techniques, these catheters are responsible for a spectacular and dramatic improvement in the management of arterial emboli, and mortality rates have been favorably influenced.

Thompson, Green, Perdue and their colleagues have described the changes in the management of arterial emboli.[93-95] Limb salvage in more than 90 percent of cases can now be achieved. Patient mortality has not decreased in all series because more seriously ill people are now considered candidates for surgical operation. Mortality rates of 10 to 15 percent are reported, but most deaths are in those patients with severe arteriosclerotic heart disease—many of whom would not have been previously considered to be candidates for surgical operation. Deaths as a direct result of surgical operation are less than 5 percent in most series.

Precise diagnosis, systemic heparinization, local anesthesia and early embolectomy are important features in this improvement. If these gains are to be consolidated, successful control of the underlying cause of the emboli must be achieved.

Cerebral Vascular Occlusive Disease

Arteriosclerotic occlusive disease of the extracranial cerebral vessels is an important cause of cerebral vascular insufficiency. Arterial dysplasia, trauma and extrinsic lesions may also produce sufficient disturbances in cerebral flow to induce cerebral ischemia. The relationship between extracranial vascular disease and stroke was obscured for many years because of the incomplete examination of the extracranial vessels. The standard pathological examination does not include direct visualization of the carotid and vertebral arteries in the neck. Patency is checked by the injection of saline and no morphological or histopathological studies are usually done. The relationship between completed strokes and preceding "small strokes" caused by recurrent episodes of cerebral ischemia was subsequently established. Many in-

vestigators, after examining these relationships, concluded that approximately half of the patients with nonhemorrhagic strokes had extracranial vascular disease.

The natural history of patients with cerebrovascular ischemia has often been misjudged. The retrospective study reported by Robinson, an evaluation of more than 1,000 patients with nonhemorrhagic stroke, showed that most patients did not get well following these episodes.[97] He reported that approximately one fifth of the patients died with the initial stroke, and of the survivors only a third eventually achieved complete recovery. The remaining people continued to have neurological disability and many also had recurrent symptoms. Acheson reported a prospective six-year study of 500 patients with cerebrovascular insufficiency.[98] Two thirds of these patients had more than one episode and only one third of the patients were free of symptoms at the end of the study period. Perhaps of more importance was the observation that of 151 patients with transient attacks of cerebral ischemia, in 60 percent a stroke eventually developed. These studies along with many others present strong evidence that the natural history of occlusive cerebrovascular disease is more dismal than suspected.[99,100] In fact, it appears clear that most people with strokes do not recover but symptoms continue and cerebral infarction is likely to develop.

Since the introduction of cerebral arteriography by Moniz in 1927 many thousands of studies have been done.[21] It is apparent that segmental arteriosclerosis and ulcerative plaques occur in the extracranial cerebral vessels as in other arteries. More than 50 percent of the patients have multiple lesions, of which some may be inaccessible. The most common patterns of involvement, however, include the presence of segmental lesions at the orifices and bifurcations of the carotid and vertebral arteries. Less frequently the intracranial portions of the basilar artery and internal carotid artery are affected. There may be, of course, associated stenotic or occlusive lesions of the great vessels at the arch.

Fields has shown that the circle of Willis as depicted in the anatomy books is intact in no more than 50 percent of patients.[101] Absence of a posterior communicating artery and variable patterns of the anterior cerebral arteries are often encountered and other congenital anomalies have been described. These collaterals have a bearing on the ability of the patient to cope with progressive stenosis and occlusion of extracranial arteries. The cerebrovascular cooperative study has elucidated the pattern of these arteriosclerotic lesions, and data derived from this study show the unfavorable influence inadequate collateral channels have on the natural history of this disease.

Careful biplane arteriograms of the intracranial and extracranial circulation, including the venous phase, have proven to be important in the proper management of cerebral vascular insufficiency. Clinical evaluation of the patients will usually provide significant clues as to the presence or absence of these lesions, but in approximately a third of the patients there may be no physical findings of extracranial vascular disease, despite it being shown by arteriograms.

The Doppler ultrasonic flow detector is useful in certain instances, especially if there is retrograde flow in the supraorbital arteries.[102] This suggests that there is occlusive disease and reduced pressure in the ipsilateral internal carotid artery. It is obvious that lesser degrees of stenosis or ulcerative plaques will not be detected by this method. Because the internal carotid is not accessible for palpation or direct examination, some form of visualization becomes imperative. Imaging techniques utilizing pulsed Doppler signals and computer analysis have shown the contours of the vessels, and may detect areas of significant arteriosclerosis. Small lesions and ulcerative plaques, however, remain beyond the definition of this technique. Similar problems are encountered with radionuclide imaging techniques, as previously described. The contours are too hazy and ill defined to allow the detection of small lesions.

Of the more innovative tests available, the new tomographic scanning technique promises to be of great value.[32] These procedures, controlled and analyzed by computer, utilize the basic principle of differing absorption of x-rays by various tissues. One may, therefore, develop cross-sectional images in which tissues with varying absorption coefficients may be separated. These studies are particularly useful in examination of the brain and especially in the detection of intracerebral hematomas and mass lesions. Further adaptation suggests that the instrument may be of assistance in assessing blood flow. It is apparent that these

newer scanning techniques will largely replace the classic brain scan. These studies are very useful in research, but their complexity and expense preclude their being used in all cases. These machines are therefore based in large diagnostic centers, and although they are of considerable value, angiography is still usually required.

On most vascular surgical services patients with cerebrovascular insufficiency are basically divided into four groups, according to types of symptoms. Some patients have transient attacks of cerebral ischemia, often called "TIA." These patients usually have transient neurologic dysfunction, often reflecting hemispheric involvement. In some cases there may be a total reduction in flow and perfusion which produces less precise symptoms. The mechanisms of production of these symptoms are thought to include the distal embolization of platelet, fibrin or atheromatous debris emanating from arteriosclerotic plaques at the bifurcation of the carotid. The emboli may also come from lesions in the aortic arch, great vessels and heart, but these are less frequent. DeBakey and his colleagues proposed the concept of "totality of cerebral blood flow," and stated that because of inefficient collateral circulation and associated segmental arteriosclerotic lesions, cerebral blood flow may fall below critical levels.[103] This perfusion defect may be aggravated by other arterial diseases, particularly heart failure and cardiac arrythmias. Hypovolemic or hypotensive episodes associated with serious illnesses or drug administration may further reduce cerebral flow. In some hypertensive patients vasospasm may occur, perhaps predisposing to the development of lacunar infarcts. All of these various disorders may, of course, cause transient attacks of cerebral ischemia and, if more severe, produce cerebral infarction.

Some patients admitted to hospital with cerebrovascular insufficiency have a progressive stroke, sometimes called a stroke in evolution. These patients have an unstable neurologic deficit and may progress to the third category, completed stroke. In some instances, however, the progressive stroke may resolve. Many patients with these changing neurologic signs have incomplete lesions, and may or may not be evolving a cerebral infarct. It is obvious that therapeutic intervention in some of these patients will evoke dramatic results, but the timing of operation is extremely important because the risk of extending a subclinical infarct is significant.

The third group of patients include those who have a completed or frank stroke and therefore are less frequently seen on a vascular surgical service. In these patients a cerebral infarct has occurred and can usually be clearly identified by examination. Diagnostic studies such as angiography may be hazardous and surgical intervention in many instances is fraught with danger. In most instances these patients are allowed to become neurologically stable before intervention is contemplated. Most vascular surgeons involved in the care of these patients believe that the severe neurologic deficit is the result of an established cerebral infarct and one is unlikely to be able to reverse the lesion. Moreover, the damage may be extended if all anemic infarct is converted to a hemorrhagic infarct. For this reason most physicians caring for these seriously ill patients recommend that the neurologic lesion be allowed to stabilize before intervention, usually requiring a period of two to four weeks.[100]

The fourth group of patients includes those who have an asymptomatic carotid bruit produced by a stenotic lesion. The indications for surgical operation in this group of patients are particularly difficult inasmuch as the natural history of all these lesions has not been adequately explored. Several provocative studies have been presented, however, the results of which strongly suggest that progression occurs in most of the patients and eventually symptoms supervene. Thompson and his associates have published data describing the natural history of more than 60 patients with carotid bruits produced by stenosis.[31] Over a five-year period strokes apparently related to this lesion developed in approximately 30 percent of these people. These data are consistent with those findings reported by Acheson.[98]

Serial angiographic studies presented by Javid are very pertinent.[104] In this careful prospective study approximately 100 patients were arteriographically examined annually to determine the natural history of carotid atheromata. Over a five-year period significant progression of the carotid atheromata was seen in 62 percent of patients, and in half of these the stenosis increased by more than 25 percent per year. Approximately a third of the patients had no change during this angiographic study. Of those patients in whom a significant increase in the stenosis was seen, signs

of cerebral vascular insufficiency developed in more than half. Progression of the lesions was more likely to occur in those patients who were hypertensive or symptomatic. Lesser degrees of stenosis progressed less rapidly. These data, combined with findings in studies presented from many vascular clinics, lend strong support to the concept that significant occlusive lesions of the extracranial carotid arteries are likely to progress to the point where they produce symptoms.[105] In most instances these will consist of transient attacks of cerebral ischemia, but some patients may have a frank stroke without the usual preceding "small strokes." For these reasons most vascular surgeons believe that preocclusive and highly stenotic lesions of the extracranial carotid artery should be repaired if the risk of operation is acceptably low.

Fields has proposed that patients in whom major vascular procedures are to be done where hypotension may be a complicating factor are very vulnerable to stroke if a tightly stenotic carotid artery is present.[104] The incidence of stroke in these patients is significantly higher and many doctors believe that in these people the carotid artery should be repaired before undertaking the major surgical procedure. An operative mortality rate of less than 0.5 percent has been reported in these patients.

Rapid changes have evolved in the operative and anesthetic techniques of carotid endarterectomy and most vascular surgery services have two distinct eras of management. Following the initial carotid operation by Eastcott, Pickering and Rob, and by DeBakey and his colleagues in 1953 carotid endarterectomy became one of the most frequently employed peripheral vascular procedures.[31] Many of the original operations were carried out under local or field-block anesthesia, permitting continuous evaluation of the neurological status of the patient. Some surgeons used the temporary inlying bypass shunt, a technique whose utility has been repeatedly proven by Thompson and his associates.[31]

Other surgeons prefer to employ general anesthesia and therefore careful attention is given to the type of anesthetic agent. It was shown that general anesthesia offered significant protection to the cerebral cortex from ischemia incurred during temporary occlusion of the carotid artery. A combination of barbituate and narcotic anesthesia combined with nitrous oxide also appears to provide some protection from cerebral ischemia. It has been shown on many occasions that patients who would not tolerate temporary occlusion of the carotid under local anesthesia do very well with general anesthesia. Halothane has been most often the anesthetic of choice.

During these studies, it became apparent that one of the most important features in the conduct of these operations was to maintain the blood pressure of the patient at or slightly above its normal level.[103] Induced hypertension, on the other hand, has proven not to be of much use and some investigators have suggested that it may actually be detrimental, producing competitive vasospasm. Similarly, it has been shown that the administration of vasoactive drugs is fraught with danger inasmuch as they may cause sudden hypotension which may produce sufficient ischemia to lead to a cerebral infarct.

The concept of utilizing hypercarbia as an adjunct to surgical procedures on the carotid artery was introduced by Wells, Keats and Cooley in 1962.[106] It has long been known that carbon dioxide and hydrogen ion concentration are important factors influencing cerebral blood flow. It was proposed by Cooley and his associates that the administration of hypercarbia during carotid occlusion would significantly increase cerebral blood flow and provide some protection from ischemia during the operation. Preliminary data supported this position, but findings in further studies by Ehrenfeld and his associates suggested that the converse might be true.[107] These workers, utilizing those principles initially described by Lassen, showed that in many patients maximum regional cerebral vasodilatation had already supervened as a result of the neurologic injury. The administration of additional carbon dioxide served only to dilate the other cerebral vessels, and when associated with fixed cerebral blood flow because of extracranial vascular lesions, the net result might be an "intracranial steal." If this situation obtained, they reasoned, hypercarbia would divert into more normal vessels a fixed volume of cerebral blood flow, and thus produce increased cerebral ischemia in the area of the recent neurologic insult. Because of these studies, and others, most anesthesiologists and vascular surgeons prefer that carbon dioxide not be manipulated, but kept within the normal range.

Although the data presented by Thompson, Gaspar and Javid strongly suggest that a tempo-

rary inlying bypass shunt is a safe and expedient method of maintaining cerebral blood flow during carotid reconstruction, other surgeons believe using the shunt may present an encumbrance to the operation.[100] It is suggested that those patients with small internal carotid arteries and highly placed carotid bifurcations are easier to manage without a shunt. It is apparent from data supplied by Wylie that in probably no more than 15 percent of patients is a shunt required during carotid endarterectomy.[100] The problem has been identification of the specific patients in whom this support is necessary. Techniques have been developed to assess this need and these include continuous electroencephalographic monitoring, a very sensitive method of determining significant reductions in blood flow.[108] Unfortunately interpretation of the electroencephalogram may be difficult, and this test does not expose ischemia occurring in the posterior circulation. Other methods of monitoring have included evaluation of ipsilateral jugular venous oxygen content. The initial reports by Lyons and his associates suggested this might be a helpful method of determining the need for additional support of cerebral circulation, but dissenting reports by Larson and Perry and associates indicated that anatomical lateralization was not consistent, and that many factors influenced the jugular venous content and saturation.[107,109] It is rarely employed today.

The most commonly used technique for evaluating the need for a shunt is to measure internal carotid back pressure in the intracranial circulation. This was initially proposed by Moore, Hall, Blaisdell and associates.[110] They suggested that an occluded "stump" pressure in the internal carotid artery of 25 mm of mercury or greater was an indication of adequate cerebral blood flow during carotid repair. If the patient had an established neurological deficit, a shunt was used regardless of pressure levels. Other data reported by Hays and co-workers suggest that the stump pressure should exceed 50 mm of mercury.[111] This is in agreement with findings in the experimental and clinical studies of Engell.[112] In patients with normal blood gas tensions and normal blood pH, an occluded distal carotid pressure of 50 mm of mercury correlates well with the blood flow requirements of the human brain, 54 ml per 100 grams of brain per minute. These studies support the concept of measurement of back pressure as a guide for the use of temporary carotid shunts.

The simple techniques initially described by DeWeese and Rob, Perry and co-workers have been useful in many vascular centers.[109,113] In this procedure the carotid artery is opened and the backflow from the internal carotid observed. If the retrograde arterial stream is brisk, bright red and pulsatile the operation is continued without the use of the shunt. In the event that the flow appears to be impeded a temporary inline shunt is inserted. It is obvious that a shunt will be employed in some cases where perhaps it is not needed, but in the view of Thompson and others this should present no problem. In fact, these very experienced investigators suggest that a shunt be used in all patients as a routine. Once facility is gained with its use it not only offers little encumbrance, but it acts as a stent to simplify the repair.

Simple endarterectomy of the carotid bifurcation is the usual procedure employed for arteriosclerosis, with careful attention to the separation of the distal plaque at the interface between normal and abnormal intima in both internal and external carotid arteries. Meticulous closure is usually satisfactory, although some surgeons prefer patch graft angioplasty. Resection and direct anastomosis or vein graft interposition is favored for treatment of dysplasia, but graduated dilatation of extensive multifocal lesions is useful in certain cases. All these procedures are very effective and quite durable.

Utilizing the techniques detailed in the preceding section, the mortality rate of carotid endarterectomy is reported in most vascular centers to be less than 1 percent. The rate of neurologic deficit incurred as a result of operation in most centers is reported as being less than 0.5 percent, although in 2 to 4 percent of the patients careful examination may show a transient deficit. It is apparent that in those patients who have a stroke in evolution higher morbidity and mortality rates may be encountered, particularly if the patients at the time of operation have a changing cerebral infarct. Most surgeons believe that operation on a patient with an acute severe stroke, particularly if associated with altered consciousness, is contraindicated. Mortality rates of up to 40 percent have been reported. It would appear that if a cerebral infarct is present, it is desirable to allow the patient to become neurologically stable before study or operation.[100] Operation for acute deficits may be useful in those patients in whom an in-

complete neurologic deficit has occurred, especially under direct observation. This may be seen in patients who are being prepared for surgical operation, after angiography or in rare cases, postoperatively. In other patients rapidly recurrent attacks of transient cerebral ischemia may be an indication for a relatively urgent operation and in some patients dramatic results have been obtained by this technique.[114] For the most part, however, emergency operations upon the stenotic carotid artery are rarely indicated.

The long-term results obtained by operation for cerebral vascular insufficiency have changed dramatically over the past decade.[31] With the current selection and management of the patients who have as presenting symptoms hemispheric signs of carotid insufficiency relief of these symptoms in more than 90 percent of cases can be expected. The late stroke rate in these patients is reported as being less than 5 percent when related to the operated artery. In those patients with more diffuse symptoms, rather than hemispheric, relief has been obtained in 60 to 80 percent of patients. The incidence of late stroke in these patients is also low, but it is well recognized that in patients who have predominantly vertebrobasilar symptoms, ultimate stroke is not as common as in those patients who present with symptoms related to the carotid territory. Nevertheless, significant improvement can be obtained in these patients if a neurologic deficit is not present at the time of operation.[100]

Of the nonsurgical methods currently used in the management of cerebral vascular insufficiency anticoagulation remains useful in some cases. Findings in studies of Baker, following a cooperative protocol, suggest that the main efficacy of anticoagulation is in those patients who have transient attacks of ischemia, apparently because of cerebral emboli.[115] Anticoagulation does not appear to be effective in the management of patients with neurologic deficits, or in progressive strokes. In fact, it is detrimental in these patients and produces a higher mortality than in the untreated group. Of more importance, however, is the current interest in the use of drugs which inhibit platelet aggregation. A cooperative study is in progress to evaluate the efficacy of aspirin in patients with cerebral vascular insufficiency. As alluded to in preceding sections there are numerous agents which are effective in reducing the tendency of platelets to aggregate and form arterial emboli, and these may be highly effective in these patients. Preliminary studies suggest this to be true but satisfactory controls have not been obtained and until the cooperative study is complete this issue is unsettled.

Visceral Arterial Disease

Arterial insufficiency as a result of stenotic or occlusive lesions in the celiac and mesenteric arteries has been described in many patients.[116] Arterial emboli have been reported to produce severe ischemia, particularly when in the superior mesenteric artery. Early identification of these syndromes is difficult and as a result morbidity and mortality rates are quite high. Recent advances in arteriographic techniques have enabled physicians to diagnose these problems at an early stage, before development of intestinal gangrene, and scattered reports of successful mesenteric artery embolectomy have appeared with increasing frequency.[116] Nevertheless, consistent diagnosis and early treatment is not often obtained. This is partly the result of associated illnesses because this syndrome is most likely to appear in people with severe cardiopulmonary disease, and in those who have low flow states produced by any cause. Nonocclusive intestinal ischemia may occur in such cases, particularly in those patients with congestive heart failure in whom digitalis is used, and in other patients when low flow occurs as a result of hypovolemia. If identified before the onset of intestinal gangrene, recovery is quite common, particularly if the underlying disease can be satisfactorily controlled. Unfortunately the serious nature of the associated disease often results in an unfavorable influence on the lifespan of the patient regardless of the outcome of the transient intestinal ischemia.

During the past decade there has been much interest focused on the concept of celiac and mesenteric artery insufficiency as a result of arteriosclerotic lesions, and in some instances extrinsic lesions producing partial stenosis of the celiac artery. Existence of a syndrome of median arcuate ligament compression of the celiac artery has been disputed for several years, and resolution of this problem is yet to be obtained.[117] Some investigators believe that because of anatomical differences the celiac artery may be located more cephalad, susceptible to compression by the median arcuate ligament of the diaphragm. It has been proposed that in these cases simple resec-

tion or incision of this ligament would release the celiac artery and allow restoration of normal blood flow. The operation has been used in many cases and in several series reported to be quite effective in relieving the vague symptoms associated with celiac artery insufficiency. Other investigators suggest that the syndrome does not occur except in association with occlusive disease in the superior and inferior mesenteric arterial systems. Szilagyi, and other investigators indicate that repair of the mesenteric artery circulation is effective and is all that is required. These workers state that they do not believe in the existence of an isolated median arcuate ligament compressing the celiac artery and producing symptoms.[118] On the other hand Stoney, Evans and others, following the initial reports by Marable, have described effective treatment of patients with visceral ischemia by operating upon entrapped celiac arteries with and without repair of mesenteric artery lesions.[119-121] It would appear, from the observations of these investigators, that ischemia in this area does occur and perhaps especially when more than one system is involved. Because of the lack of objective tests of intestinal ischemia, elucidation of this problem is incomplete. It is reasonable, however, to expect that in patients with abdominal angina, particularly those with multiple occlusive lesions, selective repair should be successful.

If visceral ischemia can be clinically identified angiograms are required for its final diagnosis and evaluation. In most cases, exclusive of those patients with emboli and the median arcuate ligament syndrome, the arteriosclerotic lesion is the typical segmental atheromata located at or just beyond the orifice. In the superior mesenteric artery this generally means in the first 2 cm of the artery, and the distal arterial bed is often, but not always spared. Once the lesion is identified and associated arteriosclerotic lesions evaluated operative repair usually consists of either thromboendarterectomy or bypass with autogenous tissue or a plastic graft. The most commonly employed solitary technique has been a bypass graft inserted end-to-side to the aorta and end-to-side to the superior mesenteric artery. Tube grafts of knitted Dacron have been most commonly employed and appear to be very effective in the management of this disease. In some cases associated arterial disease may require special techniques and more extensive reconstructive procedures.

The precise incidence of splanchnic artery aneurysms is unknown but they are apparently more common than usually appreciated, and the splenic artery is involved in more than half the cases.[122] In a review of 3,600 abdominal arteriograms where the splenic vessels were visualized, Stanley and co-workers reported 28 incidental splenic artery aneurysms, an incidence of 0.78 percent. These workers further showed that splenic aneurysms were more likely to occur in multiparous women or in young pregnant women, suggesting that the frequently observed medial degeneration was perhaps a result of hormonal influences during gestation. Arteriosclerotic splenic aneurysms do occur, but some workers have suggested that these may often be secondary to medial degeneration. An increased number of splenic artery aneurysms is seen in patients with portal hypertension and splenomegaly, and they may also occur in association with focal arterial inflammatory processes such as polyarteritis.

Assessment of the natural history of splenic artery aneurysms has prompted changes in management. The risk of rupture, except in symptomatic patients and young women during pregnancy, is less than previously thought. Stanley and his associates report a rupture rate of 5.3 percent except in these special categories.[123] Hypertension, of course, exerts an unfavorable influence, especially on large aneurysms. Because the mortality attending rupture of splenic artery aneurysms is approximately 25 percent, most vascular surgeons believe that early surgical treatment of these aneurysms is indicated if the operative mortality can be kept at an acceptably low rate, 1 percent or less. The indications for operation are more compelling in young pregnant women or in grand multiparous women. In other groups careful observation may be indicated, especially if calcification is present and the aneurysm can be followed with ease.[123]

Renovascular Disease

Lesions of the renal arteries as a cause of hypertension have received a tremendous amount of interest and research effort since the concepts were proposed by Goldblatt.[124] Although in most patients with hypertension, renovascular disease is not the cause, this is an important entity since it may yield to appropriate surgical therapy. It has been estimated that in 5 to 10 percent of patients with hypertension, renal arterial stenosis is the cause. This may constitute a significant problem, for as Foster and his associates at Vander-

bilt have reported in 1,000 hypertensive patients, renal artery lesions were found to be present in 460. Of the original series 39 percent, 176 of these patients, had renovascular hypertension.[125] This represented 16 percent of the entire group. This does not reflect the incidence of renovascular disease in the population as a whole because of the selectivity of the patient referral system. Nevertheless, it is a significant problem and deserves the special study it has received at several large centers.

Stewart and co-workers, Wylie, Foster, Fry and their associates have presented carefully detailed studies of the histopathological and morphological features of the lesions producing renovascular hypertension.[125-127] The pathological lesions can be divided into two groups, intimal and medial.[128,129] In the former group segmental stenosis is caused by atherosclerosis and intimal fibroplasia. Of those lesions involving the media of the artery, fibromuscular hyperplasia, medial fibroplasia and subadventitial fibroplasia are common. Associated extrinsic lesions may be found on occasion and intrarenal lesions may also be found, particularly with collagen diseases such as periarteritis. Trauma and renal infarcts and other retroperitoneal lesions may induce renal ischemia and subsequent renovascular hypertension, but are relatively uncommon.

From a functional point of view, rather than to divide the lesions according to pathologic findings it has been found more convenient to divide the lesions according to their morphologic characteristics.[129,130] Such a classification has importance both diagnostically and in regard to the natural history of the lesions. This classification divides them into three groups; focal, tubular and multifocal. Atherosclerosis, intimal fibroplasia and fibromuscular hyperplasia may produce focal lesions of the renal artery. The tubular lesions are usually caused by atherosclerosis and subadventitial fibroplasia. Atherosclerosis, medial fibroplasia and subadventitial fibroplasia may cause multifocal lesions, particularly common in the renal arteries. Medial fibroplasia produces the familiar "chain of lakes" or "string of beads" radiographic pictures so commonly associated with arterial dysplasia, and often erroneously called fibromuscular hyperplasia. There is no true hyperplasia in this variety, only dysplasia.

The natural history of these lesions is of extreme importance when deciding upon the indications for operative intervention.[130] As anticipated, the atherosclerotic lesions tend to progress, consistent with those changes occurring in other arteries. Unfortunately these lesions tend to occur in older patients and in those who have diffuse arterial disease. Therefore, the overall prognosis is somewhat less favorable than that encountered in patients with dysplastic lesions. Nevertheless, significant atherosclerotic lesions producing sufficient disturbances in renal blood flow to induce renovascular hypertension and posing a threat to the viability of the kidney may present compelling indications for operative intervention.

In those patients with renal dysplasia the focal lesions tend to proceed inexorably toward occlusion regardless of the underlying pathologic entity. In most cases these patients are younger and have renovascular hypertension. These lesions are particularly subject to local occlusion, intramural dissection, mural hemorrhage and in some patients malignant hypertension. Because of the tendency toward progression early operative treatment is indicated in most of these patients.[128-130]

In some patients with medial fibroplasia and multifocal lesions operative intervention will be indicated because of associated renovascular hypertension or threatened viability of the kidney. When encountered in its later stages, however, progression of this particular variety does not appear to be as rapid or as predictable as that of the focal lesions. If satisfactory blood pressure control can be obtained and renal viability is not threatened, nonoperative therapy may be successfully employed in these patients. Surgical intervention may occasionally be required at a later date, and repeated screening and angiographic procedures may be necessary in order to adequately follow the course of the disease. Assessment of the natural history of these lesions is of extreme importance in determining the requirements for operations. As has been pointed out by Foster and others, bilateral lesions tend to be metachronous and renal preservation is extremely important.[125] Nephrectomy as a primary mode of therapy is generally not indicated, since the surgeon may later be confronted by a severe lesion in the remaining kidney. Technical repair may not be possible at this later date. Every effort should be made to conserve renal tissue and early operation may reduce the risk of losing the kidney.

The diagnosis of renovascular hypertension remains difficult in some instances, but recent im-

provements in functional evaluation have been achieved. In most cases the diagnosis centers on the exposure of a significant arterial lesion and then subsequent proof of its functional activity. Those data reported from the University of California, San Francisco, in regard to arterial dysplastic lesions have suggested that more than 95 percent of patients can be cured of their renovascular hypertension when these lesions are identified at an early enough age and successfully repaired.[131] Functional tests, although obtained in these patients, have not been used in determining the need for operation. In most cases, and especially in those patients with atherosclerosis and multifocal lesions, assessment of the functional activity of the anatomic lesion is desirable before operation.[129,130]

The pioneering work of Howard and Stamey in evaluating bilateral renal function has been extremely useful, but these tests are not now used as often as in the past. Investigators at Vanderbilt still use split function tests in association with other studies and suggest that they have considerable value.[125] Newer tests of renal function, as reported by DeGrazia, utilize sophisticated isotopic techniques which allow simultaneous discrimination of renal excretory function and renal plasma flow.[132] These studies, while somewhat expensive, promise to be of great value in studying renovascular hypertension, and have the advantage of not requiring cannulation of vessels, or ureteral intubation. Numerous procedures have been proposed for the evaluation of renovascular hypertension, but most vascular centers caring for these patients have a protocol which employs the more reliable and simpler tests. It is apparent that more than the intravenous pyelogram (IVP) is necessary because it will indicate only about a third of those patients in whom renovascular hypertension is later shown to exist. The most commonly employed diagnostic protocol is similar to that devised at the hypertension center at Vanderbilt, and includes a 24-hour urine specimen for measurement of creatinine clearance, electrolytes, cathecholamines, vanillyl mandelic acid, 17 hydroxy steroids and ketosteroids. Subsequently a rapid sequence urogram is obtained and then renal arteriography and renin assay.[125]

The determination of plasma renin activity is important both in diagnosis and in establishing the prognosis in these patients. There are various techniques used in these studies, but the object of the test is to detect an increase in renin production from the affected kidney. This may be augmented by salt depletion, administration of hydralazine, bringing the patient into the erect position or by other provocative maneuvers. The basic aim is to show when there is an increased renin production by the affected kidney and then confer upon the anatomical lesion functional activity. In those patients who have unilateral disease a renal vein renin ratio between abnormal and normal of 1.4 or greater is often sought, but it has been recognized that autonomy may develop in some patients.[133] Peripheral renin activity may be normal and renal vein renin levels may be normal, even though an arterial lesion correctable by surgical operation is present. This is particularly likely to be the case when functioning arterial collaterals can be shown. Such arteriographic features are of considerable diagnostic importance. False negative findings, therefore, do occur in a small number of cases, and although the determination of plasma renin activity is the test for renovascular hypertension, it is not infallible.

The physiologic basis for the determination of plasma renin activity centers around the production of renin by the juxtagomerular apparatus adjacent to the afferent artery.[134] This substance is secreted into the kidney and into the lymph, and subsequently acts upon an alpha-2-globulin to produce angiotensin I, a decapeptide. Plasma and pulmonary converting enzymes act upon this decapeptide and produce the octapeptide angiotensin II. This is the active pressor agent which ultimately acts to increase arterial resistance. In addition, it stimulates the production of aldosterone and in a short loop negative feedback mechanism decreases its own production. It is subsequently hydrolyzed by peptidases into peptides and amino acids and thus rapidly destroyed.

Renin release is largely under the control of three different mechanisms. There are intrarenal receptors which are directly responsible for the production of renin and the renal nerves exert a modulating influence on this activity. In addition, certain humoral agents affect the production of renin and generally act in concert with those other processes. Most investigators agree that the vascular receptor within the wall of the afferent arteriole is dominant in this relationship and responds to changes in transmural pressure. This effect is modulated by the renal sympathetic nerve activity and by intrinsic myogenic factors, and

also may be subject to changes produced by alterations in elastic components of the wall. Nevertheless it appears that changes in wall tension are largely responsible for renin release.[134]

The macula densa apparently harbors a sodium sensitive mechanism which, according to some investigators, effects a nephron by nephron control of blood flow by responding to changes in sodium concentration in the distal renal tubule. This mechanism can be shown to be independent of the activity of the vascular receptor, but appears to have a less prominent role in renin control. Catecholamines, steroids, sodium and potassium ions all may influence renin production. Angiotensin II and antidiuretic hormone (ADH) are also involved in a short loop negative feedback system.

Initially the management of renovascular hypertension in patients with unilateral lesions was nephrectomy, and this was often an effective mode of therapy. Because of metachronous lesions, however, it is no longer acceptable to resect the kidney except in those instances in which repair may not be possible. Freeman and Wylie pioneered in renal artery reconstruction by endarterectomy, but the bypass techniques have proven to be more popular among most vascular surgeons.[130] Transaortic renal endarterectomy and appropriate repair with or without angioplastic techniques have been very useful. Autogenous and plastic prosthetic aortorenal bypasses are currently the most commonly used procedures. As mentioned in previous sections, the late behavior of these antogenous bypasses introduces some cause of concern, especially because uniform dilatation has supervened in a few patients. Only a very small proportion, 2 to 4 percent, have become aneurysmal, and these appear stable.[48,49] Serial angiographic procedures are currently in progress to investigate the long-term behavior of these arterial conduits, and there is considerable discussion as to which type of autogenous tissue is most useful, saphenous vein or hypogastric artery. The issue at present is unsettled as both appear to be very useful in the management of these diseases, complications occurring in only a very few cases.[125,128,131] In some patients aortorenal bypasses done using Dacron prosthetic implants have also been effective, and many large centers report excellent long-term behavior of these grafts.

It is apparent that those patients who have fibromuscular dysplasia can be expected to respond satisfactorily to this operation, and success rates exceeding 95 percent have been reported from many institutions. In contrast are those patients with multifocal lesions in whom the results of operation are less dramatic.[129] Nevertheless, substantial gains can be expected, and up to two thirds of the patients can be benefited by appropriate repair techniques. In some, the administration of small amounts of antihypertensive drugs may be required in order to maintain satisfactory blood pressure levels. In addition, preservation of renal tissue is possible in many of these cases and there are persuasive data indicating that in many cases it has been possible to avoid nephrectomy because of new developments in reconstructive techniques.

Autotransplantation with temporary perfusion of the kidney, techniques developed during renal transplantation, have enabled vascular surgeons to repair lesions in small renal artery branches which previously would not yield to other techniques. Operations have been reported by Lim, Foster and others and it is apparent that before removing even what initially appears to be an inoperable kidney, these exogenous repair techniques should be undertaken.[135,136] In many cases they will enable vascular surgeons to preserve a kidney which would otherwise be doomed to nephrectomy.

Special techniques have been successful in treating renal arterial dysplasia. Graduated dilatation is useful here, as in other arteries, and especially in small branches.[137] If resection and replacement are not feasible, such intraluminal remodeling may be very helpful. Microsurgical procedures are of particular use in these cases, and their application is facilitated by autotransplantation techniques.

Several large centers have now reported on results 10 years after renal artery reconstruction. The initially successful effect has been sustained in most instances, and if contralateral disease has not supervened, the results of these operations have proven to be remarkably durable. This is especially likely in those patients with medial dysplasia. The reports of the cooperative study on renovascular hypertension showed that of 502 patients with renal artery stenosis and coexisting hypertension, following repair 51 percent were cured, 15 percent were improved and 34 percent failed to respond.[138,139] The operative mortality was 5.9 percent. With unilateral fibromuscular

disease a favorable blood pressure response was seen in 79.8 percent while in those with unilateral arteriosclerosis 63 percent were benefited. In those patients with bilateral stenosis a favorable result occurred in only 56 percent. From the data recovered from this study certain conclusions are presented, suggesting corrective surgical procedures are especially useful in unilateral disease when there is evidence of functional renal disparity judged by various diagnostic tests. In patients who have bilateral renal artery stenosis, repair is frequently effective and the side with the greatest functional disturbance should be initially reconstructed. Subsequently, the decision to repair the other side would be determined by the patient's response and the results of the various tests. The directors of the cooperative study concluded by indicating that in their opinion an operative procedure should be considered in patients who have moderate to severe hypertension that is refractive to drug therapy, and in people in whom preservation of renal tissue is an important consideration.[139]

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Perils of Oxygen Toxicity in Treating the Adult Respiratory Distress Syndrome

One tries to deliver oxygen to patients with adult respiratory distress syndrome but one cannot give oxygen with impunity . . . I think it's now safe to say that the administration of high concentrations of oxygen for more than three or four days will lead to lung damage. In fact, in one study carried out in our hospital, one could get physiological evidence of impairment of pulmonary function after 36 hours of administration of 100 percent oxygen.

One should bear the familiar oxyhemoglobin dissociation curve in mind, and one key number to remember, because it's very useful clinically, is an arterial oxygen pressure (Po_2) of 60. A value of 60 is at the shoulder of the curve and is approximately 90 percent saturation. So that if your Po_2 is over 60, you're in pretty good shape in terms of providing about as much oxygen to that amount of blood as it can contain. And there's no sense having a Po_2 of 300 because that adds very little more oxygen to the bloodstream and has a much greater injurious effect on the lung. So try to keep Po_2's in the neighborhood of 60—and in some of these patients 60 is a luxury and more than you can get and sometimes you have to settle for 50 or even 40. Another important number to remember is 40, which is 75 percent saturated. If you're using mixed venous oxygen tension as a guide to adequate delivery of oxygen, the number we use clinically is about 30 mm of mercury. We'd like to have it higher than that. Again, sometimes it's difficult to achieve this value.

—DICK D. BRIGGS, JR., MD, *Birmingham, Alabama*

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